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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/380,310	08/31/1999	KOJI UKAI	425-736P	2449

2292 7590 02/26/2007

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EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	**PAPER NUMBER**
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	02/26/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 02/26/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	09/380,310	UKAI ET AL.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-9,13-16,20-22,25,28-30,35-37,40-53,55-59 and 61-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 6-9, 13-16, 20-22, 25, 28-30, 35-37, 40-53, 55-59 and 61-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of amendments and response filed 12/01/06. Claims 1, 2, 8, 9, 15, 16, 22, 25, 28, 29, 30, 37, 41, 42 and 43 have been amended. Accordingly claims 1, 2, 6-9, 13-16, 20-22, 25, 28-30, 33-37, 40-53, 55-59 and 61-63 are pending.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 2, 6-9, 13-16, 20-22, 25, 28-30, 35-37, 40-53, 55-59 and 61-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tai (5,013,557) in view of Kawakami et al (The Rational for E2020 as a potent acetylcholinesterase inhibitor).

Tai discloses taste masking compositions comprising spray dried microcapsules containing sucralfate and methods for preparing same. The spray dried spheroidal microcapsules comprise in percentages by weight between 1 and 70% of **sucralfate** and between 30 and 99% of a polymer soluble in gastric fluids (col. 5, lines 30-60). The **polymers soluble in the gastric fluids** are polymers which **bind to sucralfate** with taste masking properties and dissolve in gastric fluid. The suitable polymers include alginic acid, **carrageenan**, xanthan, etc (col. 6, lines 26-55). Tai lacks specific disclosure on donepezil hydrochloride as the active agent.

Kawakami et al teach E2020 (also known as donepezil hydrochloride) as a potent acetylcholinesterase inhibitor. E2020 was developed for treatment of Alzheimer's disease, and possibly other dementias.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the formulations of Tai containing a basic medicine with unpleasant taste and an acidic polysaccharide such as carrageenan with other active agents such as donepezil hydrochloride as taught by Kawakami et al in order to prepare more drug formulations with a masked taste for patient convenience and to increasing patient compliance. In other words, one or ordinary skill in the art having the formulations of Tai, would have been motivated to apply the same method to other medications with unpleasant taste in order to provide better tasting medication for patients and increase patient compliance.

Claims 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tai (5,013,557) in view of Kawakami et al (The Rational for E2020 as a potent acetylcholinesterase inhibitor) as applied to claims 1, 2, 6-9, 13-16, 20-22, 25, 28-30, 33-37, 40-53, 55-59 and 61-63 above, and further in view of Morikazu et al (JP 4-346937).

The combined references, discussed above, lack specific disclosure on derivatives of carrageenan.

Morikazu teaches a method of simply and economically reducing bitterness of drugs and foods. For that, Morikazu mixes a bitter substance with a gelatininzing agent such as gelatin, *k*-carrageenan, etc and a seasoning agent, preferably a sweetener (see abstract).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have implemented the gelatinizing agents such as *k*-carrageenan as taught by Moikazu into the drug formulations of the combined references with the reasonable expectations of successfully preparing a safe and effective drug formulation without a bitter or unpleasant taste for patients that need such medicaments.

Claims 1, 2, 6-9, 13-16, 20-22, 25, 28-30, 33-37, 40-53, 55-59 and 61-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Diehl (5,612,026) in view of Kawakami et al (The Rational for E2020 as a potent acetylcholinesterase inhibitor), and further in view of Morikazu et al (JP 4-346937).

Diehl discloses drink mix compositions comprising a therapeutically effective dose of an **anionic exchange resin**, from about 0.05 to about 1.25g of xanthan gum and an edible, water soluble salt (col. 2, lines 13-17). The anion exchange resin means any resinous material having cationic moieties, such as *cholestyramine* and *colestipol* hydrochloride, both of which are strongly basic anion exchange resins (col. 3, lines 15-

30). Diehl also discloses that edible water soluble salts MAY be added (col. 3, lines 48-62). Other materials including bulking agents and carriers may be added. Such materials can be oligosaccharides and **polysaccharides** (col. 5, lines 20-45). The resulting dosage form is typically granules (col. 6, lines 62-67).

Diehl also discloses a method of preparing the said formulations, where cholestyramine, xanthan gum and maltodextrin are charged and allowed to mix (col. 6, lines 45-67). Diehl lacks specific disclosure on other basic medicines and other specific polysaccharides for the said formulation.

Kawakani teaches doenepezil hydrochloside and Morikazu teaches polysaccharides such as *k*-carrageenan for mixing with bitter medicines.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have substituted one basic active agent for the other as taught by Kawakami et al in order to benefit from the masking properties for more medications with unpleasant taste. Furthermore, one of ordinary skill would have been motivated to have looked for other suitable agents for assisting with masking of bitter tastes of some medicaments as taught by Morikazu. In other words, one of ordinary skill would be motivated to look for other suitable medicinal components with unpleasant taste and other suitable agents for masking the taste to implement the same method for them in order to provide the same benefit for more patients.

Response to Arguments

Applicant's arguments filed on 12/01/06 have been fully considered but are not persuasive.

Applicant states that prior to 1997 one of ordinary skill in the art was not aware of the bitter or unpleasant taste of donepezil hydrochloride, thus Applicant concludes that "the requisite motivation is lacking with regard to the examiner's combination of Tai '557 and Kwakami". This is not persuasive. Firstly, Applicant states that "Aricept, a tradename of donepezil hydrochloride, was admitted in November of 1996 by FDA in the form of a film tablet". This by itself is a showing that it was actually known to one of ordinary skill in the art at the time, i.e. 1996 or before, that donepezil hydrochloride had an unpleasant taste. Film coating is typically used on medicines for the purpose of masking bad taste. Secondly, many prior arts such as Tai, Diehl, etc, have disclosed that bad tasting medicines need taste masking agents to assist patient's tolerance of such medicines. Tai teaches that sucralfate, a basic medicine, having unpleasant taste, is mixed with a polymer soluble in gastric fluid such as carrageenan, maltodextrins, alginic acid, etc to mask the unpleasant taste of sucralfate. Diehl et al teach that cholestyramine or cholestipole hydrochloride, basic anion exchange resins, have an unpleasant, astringent taste and a gritty texture. Diehl discloses that combining an anion exchange resin, such as cholestyramine or colestipole hydrochloride, with xanthan gum and maltodextrin aid in masking the unpleasant taste and mouthfeel associated with these resins. Therefore substituting one active agent for another does not alter the

scope of the invention. In other words the instant claims are obvious variations of the prior art teachings and are not patentably distinguished.

Applicant argues that the present invention is directed to administering donepezil hydrochloride together with the specific acid polysaccharides. Donepezil hydrochloride is basic and is positively charged. The acidic polysaccharides are acidic and are negatively charged, but are not sweet in taste. Applicant then concludes that "the present invention works by forming the mentioned ion complex as a way of masking the bitter taste of donepezil hydrochloride". However, the position of the office is that the prior art references are teaching the same. In Tai a basic medicine, being positively charged is mixed with an acidic polysaccharide that is negatively charged. In Diehl a basic medicine having an anion exchange resin is mixed with one or more acidic polysaccharides. Kawakami teaches E2020 (donepezil) as a potent acetylcholinesterase for treating Alzheimer's disease. Thus the combination of references produces the same formulation as that of the instant claims.

Applicant argues that Tai teaches a spray-dried product, and the taste-masking action is caused by a matrix imposed on microcapsules. This is not commensurate with the scope of claims. Instant claims are drawn to "an oral medicine composition... comprising a mixture of a basic medicine and an acidic polysaccharide....". This was taught by Tai. Instant claims do not exclude microcapsules, matrix or spray-dried products. Instant claims also use the open ended language of comprising, thus the use of other excipients such as sweeteners is permitted.

Applicant argues that JP '937 does not disclose basic medicines. This is not persuasive. JP '937 was a supportive reference in an obviousness rejection which is to provide what is lacking in the primary reference. The primary reference, while disclosing use of carrageenan as a suitable polysaccharide, lacks disclosure on specific carrageenans and JP '937 teaches the use of such specific carrageenans to aid in taste making of bitter medicinal substances.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found **either** in the references themselves **or** in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, there is sufficient in Tai and Diehl to look in the art for other active agents such as donepezil hydrochloride and other polysaccharides such as *k*-carrageenan.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mina Haghighatian
Patent Examiner
February 16, 2007

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